RESEARCH ARTICLE / *Araştırma Makalesi*

Polypharmacy in Outpatients with Bipolar Disorder: Associated Factors and Treatment Characteristics in Türkiye

Türkiye'de Bipolar Bozukluk Tanılı Ayaktan Hastalarda Polifarmasi: Tedavi Özellikleri ve İlişkili Faktörler

Neriman Aras[1], Fatma Çoker[2], Nihan Küçük[3]

[1] *Samsun Mental Health and Disorders Hospital, Samsun, Türkiye*
[2] *Hospital of Grand National Assembly of Türkiye, Ankara, Türkiye*
[3] *Department of Medical Pharmacology, Faculty of Medicine, Hitit University, Corum, Türkiye*

Yazışma Adresi / *Correspondence:*
Neriman Aras
Kadikoy Mahallesi 1545.Cadde. No:6 Ilkadim, Samsun, Türkiye
T: **+90 505 576 32 10** E-mail **: neriaras@hotmail.com**

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Orcid ve Mail Adresleri
Neriman Aras https://orcid.org/0000-0001-7410-2497, neriaras@hotmail.com
Fatma Çoker https://orcid.org/0000-0002-3818-8796, fatmacoker@gmail.com
Nihan Küçük https://orcid.org/0000-0002-9205-1467, nihankk@yahoo.com

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Abstract

Introduction	Polypharmacy is frequently used in the treatment of bipolar disorder. We aimed to investigate polypharmacy rates, associated factors, and the types of drugs preferred in treatment among outpatients with bipolar disorder.
Materials and Methods	A total of 209 bipolar disorder patients attending an outpatient psychiatry clinic were included in this study. Drug types, active substances, and combination forms were examined.
Results	The rate of polypharmacy among bipolar outpatients was found at 79.40%. Antipsychotics were the most frequently preferred drug for the treatment. The most commonly used antipsychotic was quetiapine, whereas the mood stabilizer was sodium valproate and the antidepressant was paroxetine. The most common form of treatment for bipolar disorder was the combined use of a mood stabilizer and an antipsychotic.
Conclusion	In contrast to treatment guidelines, polypharmacy has virtually become a standard in the treatment of bipolar disorder. It appears that the adoption of polypharmacy in treatment will persist for a variety of reasons. As such, there is a need to develop new guidelines to guide psychiatrists in determining the patient groups and types of combinations in which combination therapy will be preferred. Moreover, interventions are needed to minimize the possible side effects, and risk of drug-drug interactions related to the use of multiple drugs, determine the benefit/harm ratio, and reduce unnecessary psychotropic drug use.
Keywords	Bipolar Disorder; Outpatients; Polypharmacy; Drug; Treatment; Combination

Öz

Amaç	*Bipolar bozukluk tedavisinde polifarmasi sıklıkla kullanılmaktadır. Bu çalışmada, bipolar bozukluk tanılı ayaktan hastalarda polifarmasi oranlarını, ilişkili faktörleri ve tedavide tercih edilen ilaç türlerini araştırmayı amaçladık.*
Yöntem ve Gereçler	*Bu çalışmaya bir ayaktan psikiyatri kliniğine devam eden 209 bipolar bozukluk tanılı hasta dahil edildi. Tedavide tercih edilen ilaç türleri, etken maddeler ve kombinasyon şekilleri incelendi.*
Bulgular	*Bipolar bozukluk tanılı ayaktan hastalarda polifarmasi oranı %79.40 bulundu. Tedavide en sık kullanılan ilaç grubu antipsikotik ilaçlardı. En fazla tercih edilen antipsikotik ketiapin, en sık kullanılan duygudurum dengeleyici sodyum valproat ve en sık kullanılan antidepresan paroksetin idi. Bipolar bozukluk için en yaygın tedavi şekli, bir duygudurum dengeleyici ve bir antipsikotik kombinasyonuydu.*
Sonuç	*Tedavi kılavuzlarında önerilenin aksine, bipolar bozukluk tedavisinde polifarmasi standart tedavi haline gelmiştir. Bipolar bozukluk tedavisinde polifarmasi uygulaması çeşitli nedenlerle devam edecek gibi görünmektedir. Bu nedenle, polifarmasi tercih edilecek hasta grupları ve kombinasyon türlerinin belirlenmesinde psikiyatristlere yol gösterecek yeni kılavuzların geliştirilmesine ihtiyaç vardır. Ayrıca polifarmasiye bağlı olası yan etkileri ve ilaç-ilaç etkileşimi riskini en aza indirecek, kar/zarar oranını belirleyecek ve gereksiz psikotrop ilaç kullanımını azaltacak müdahalelere ihtiyaç vardır.*
Anahtar Kelimeler	*Bipolar Bozukluk; Ayaktan Hasta; Polifarmasi; İlaç; Tedavi; Kombinasyon*

INTRODUCTION

Bipolar disorder is characterized by manic, hypomanic, and depressive episodes, evolving with remissions and relapses and requiring lifelong treatment, which affects 1 to 2% of the adult population.[1-3] This complex nature of the disorder often renders the treatment process complicated and challenging for clinicians.[4] The pharmacological treatment aims to keep acute episodes under control, prevent relapses and recurrences, maintain remission for a long time and increase functionality.[1-3] Depending on the severity of the disorder, a mono- or multi-drug therapy may be administered. Yet, the disorder often requires a long-term, multi-drug regimen.[1-3,5,6]

Polypharmacy means combining two or more psychotropic drugs in the treatment of bipolar disorder, which may involve mood stabilizers (MS), antipsychotics (AP), antidepressants (AD), and benzodiazepines (BDZ), at any period of the disease.[1,7,8] Although numerous clinical guidelines have been developed, following these guidelines is not feasible in actual practice.[4]

Although multi-drug use is common and there are studies examining the characteristics and drug types associated with polypharmacy in bipolar disorder in the world, studies in Türkiye are limited.[7] In this study, we aimed to examine the rates of polypharmacy, psychotropic drugs and combination forms in bipolar patients followed up in a psychiatry outpatient clinic and to present the drugs preferred in the treatment of bipolar disorder in Türkiye.

MATERIALS and METHODS

Sample and design

This study was conducted at an outpatient psychiatry clinic, between Jun to December 2021. Two hundred eighty four patients with bipolar disorder were followed up in the outpatient psychiatry clinic. Patients with mental retardation or neurological disease and who did not want to be participate to the study were excluded from the study. According to the inclusion and exclusion criteria, 209 patients with bipolar disorder, who were clinically stable, and medical treatment remained unchanged over the past 6 months were included in the study.

The diagnosis of bipolar disorder was confirmed by a psychiatrist according to the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) criteria.[9] Ethics committee approval was obtained from the Clinical Research Ethics Committee of Samsun Training and Research Hospital with the date of 15.05.2021 and the number GOKA/2021/10/5. Written consent was observed from all patients.

MATERIAL and METHOD

The researchers created a sociodemographic data form that included age, gender, education level, duration of the disorder, and the number of hospitalizations. Also, a medical follow-up form was drawn up, which included the treatment characteristics. This study was conducted retrospectively from the medical records of patients followed in an outpatient psychiatry center.

Data analysis

The data were analyzed using SPSS 25.0. The descriptive statistics were reported as mean±standard deviation for continuous numerical variables with normal distribution. All categorical variables were presented as the number of cases (n) and percentage (%).

RESULTS

Sociodemographic characteristics

The mean age of the participants was 46.6±13 years, and the mean duration of the disorder was 17.7±10 years. The majority of the subjects were female. Over half of the patients were, at least once, hospitalized. The mean number of drugs used daily was 2.3±10. The patients' sociodemographic characteristics are presented in Table 1.

Table 1: Sociodemographic and clinical characteristics of the patients

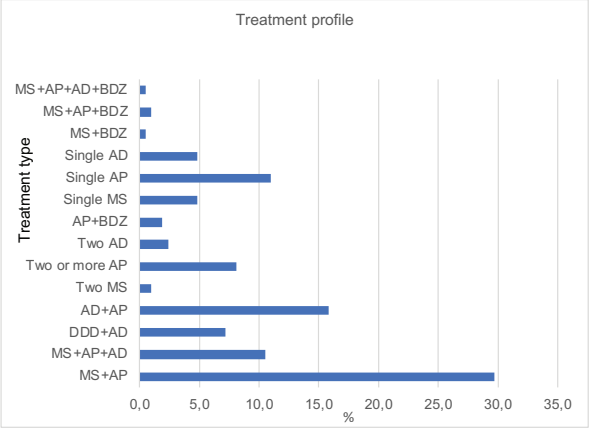
	Number (n)	Percent (%)
Sex		
Male	92	44.0
Female	117	56.0
Age		
24 years and under	10	4.80
25-34	29	13.90
35-44	52	24.90
45-54	59	28.20
55-64	36	17.20
65 years and older	23	11.0
Marital status		
Married	108	51.70
Single	64	30.60
Widowed	36	17.20
Divorced	1	0.50
Education		
Illiterate	12	5.70
Literate	3	1.40
Primary school	82	39.20
Middle school	33	15.80
High school	44	21.10
University	35	16.70
Occupation		
Employed	52	24.90
Unemployed	122	58.40
Retired	27	12.90
Disabled retired	8	3.80
Disease duration		
0-5 years	22	10.50
6-10 years	37	17.70
10 years and over	150	71.80
Hospitalization		
None	101	48.30
1-2 times	63	30.10
3-4 times	24	11.50
5 times and more	21	10.0
Hospitalization in the last 1 year		
No	196	93.80
Yes	13	6.20
Total	209	100.0

The mean age	46.6±13 (min 18, max 79 years)
The mean age of disease onset	29.2±13 (min 14, max 69 years)
The mean duration of illness	17.7±11 (min 1, max 57 years)
The mean number of hospitalization	1.8±35 (min 0, max 20 times)
The mean number of drugs	2.3±10 (min 1, max 6 drugs)

Treatment pattern

The polypharmacy rate of bipolar outpatients was 79.40%. The treatment often consisted of two or three different drugs (36.80% and 29.70%, respectively).

The widest form of polypharmacy was the combination of a MS and an AP, followed by the combination of an AP and an AD in the second, and the combination of a MS, an antipsychotic, and an antidepressant in the third. The characteristics of the patients' treatment patterns are shown in Figure 1.



**MS: Mood stabilizer, **AP: Antipsychotics, ***AD: Antidepressants, ****BDZ: Benzodiazepines*

Figure 1: Treatment profile

Types of drugs

The APs were the most frequently preferred drugs in the treatment of bipolar disorder (78.0%), followed by the MSs (54.10%). The rate of AD use was 43.50% and BDZ use was 3.80%. By active substance, the most preferred drug

was quetiapine, followed by sodium valproate and aripiprazole (37.30%, 27.30%, and 21.50%, respectively). Lithium and olanzapine ranked fourth with an equal rate of use (20.60%, each). Of the patients using antipsychotics, 92.60% were using atypical APs, and of the patients using ADs, 56.0% were using ADs from the SSRI.

Mood stabilizers

The rate of MS use was 54.10%. The most common preferred MS was sodium valproate (27.30%), followed by lithium second (20.60%). Lamotrigine or carbamazepine was less (9.10% and 5.70%, respectively).

Antipsychotics

The rate of patients using at least one AP was 78.0%, of which 48.80% were using only one AP and 29.20% of the two or more APs. Most of the APs were atypical APs (77.0%). The most preferred AP was quetiapine (37.30%), followed by aripiprazole and olanzapine, (21.50% and 20.60%, respectively).

Antidepressants

The rate of AD use was 43.50% in bipolar disorder. Of 38.30%, have one AD, whereas 5.30% had two different ADs. Patients whose treatment includes AD, 8.10% were not taking any MS or AP. Most of the ADs were SSRIs (22.50%), whereas SNRIs were 14.40%, and SSRIs+SNRIs were 1.40%. The rates of TCAs and other ADs were fairly low (5.20%). Among SSRIs, the most preferred drug was paroxetine (8.60%), and duloxetine (8.10%) was in SNRIs.

Benzodiazepines

The use of BDZ was fairly low (3.80%). The most frequently preferred was lorazepam (1.40%). Treatment patterns and types of drugs were shown in Table 2.

Table 2: Drug categories and active substances

	Number (n)	Percent (%)
Mood Stabilizer		
No	96	45.90
Yes	113	54.10
Na valproate	57	27.30
Lithium carbonate	43	20.60
Carbamazepine	12	5.70
Lamotrigine	19	9.10
Number of Mood Stabilizers		
None	96	45.90
Single MS	96	45.90
Two of MSs	17	8.10
Antipsychotic		
No	46	22.0
Yes	163	78.0
Risperidone	25	12.0
Olanzapine	43	20.60
Quetiapine	78	37.30
Clozapine	2	1.0
Aripiprazole	45	21.50
Paliperidone	16	7.70
Amisulpiride	13	6.20
Haloperidol	7	3.30
Others (Chlorpromazine, zuclopenthixol, pimozide, trifluoperazine)	8	3.80
Number of Antipsychotic		
No AP	46	22.0
Single AP	102	48.80
Two of APs	52	24.90
Three of APs	7	3.30
Four of APs	2	1.0
AP group		
No AP	46	22.0
Atypical AP	151	72.20
Typical AP	2	1.0
Atypical+Typical AP together	10	4.80
Antidepressant		
No	118	56.50
Yes	91	43.50
Only SSRI	45	21.50
SSRI+Other AD	2	1.0

Only SNRI	27	12.90
SNRI+Other AD	3	1.50
SSRI+SNRI	3	1.40
Only other ADs (TCA, mirtazapine, bupropion, vortioxetine, etc.)	11	5.20
Number of antidepressants		
No AD	118	56.50
Single AD	80	38.30
Two of ADs	11	5.30
Type of antidepressant		
No AD	118	56.60
Yes	91	43.50
SSRI		
Sertraline	15	7.20
Paroxetine	18	8.60
Escitalopram	10	4.80
Citalopram	3	1.40
Fluoxetine	2	1.0
Fluvoxamine	3	1.40
SNRI		
Duloxetine	17	8.10
Venlafaxine	15	7.20
Other ADs		
Mirtazapine	4	1.90
Clomipramine	7	3.30
Amitriptyline	2	1.0
Bupropion	2	1.0
Vortioxetine	3	1.40
Milnacipran	1	0.50
AD use without MS or AP		
No	192	91.90
Yes	17	8.10
Benzodiazepine		
No BDZ	201	96.20
Yes	8	3.80
Lorazepam	3	1.40
Alprazolam	1	0.50
Diazepam	2	1.0
Clonazepam	2	1.0
Total	209	100.0
*MS: Mood stabilizer, **AP: Antipsychotic, ***AD: Antidepressant, ****BDZ: Benzodiazepine High rates are shown in bold style.		

Variables associated with monotherapy/polypharmacy

No statistically significant differences were found between the monotherapy and polypharmacy groups for age, gender, marital status, education attainment, occupational status, age of onset of the disorder, duration of the disorder, hospitalization, number of hospitalizations, use of extended-release antipsychotics, and benzodiazepines ($p>0.05$). Hence, the age was notably higher in the polypharmacy group ($p=0.007$).

DISCUSSION

In this study, the polypharmacy rate of bipolar outpatients was 79.40%. Although not recommended in treatment guidelines, numerous studies have shown that polypharmacy is widely preferred.[3,10] In addition, there are also studies reporting that polypharmacy may be more effective than monotherapy.[11] The studies on bipolar disorder showed that the rates of polypharmacy range from 50 to 93.7%.[1,3-5,8,11-14] The discrepancies between the results reported in similar studies may be accounted for by methodological aspects (e.g., classification of drugs, sample size, drug classes, countries' treatment policies, and physicians' treatment practices).[15,16]

Sociodemographic data

The majority of patients included in the study were female (56.0%). In general, the prevalence of bipolar disorder is equal in males and females. Yet, some studies about treatment patterns indicated that the disorder is more prevalent in females.[1,4,5,8,12,17-19] It is also noted that the higher number of females may be because women are more compliant with the treatment.[5] The high number of female subjects in our study may be attributed to the women being more likely to adhere to the treatment as compared to men.

In the present study, 51.70% of the patients were married and 39.20% had primary education. Studies on the characteristics of treatment for bipolar disorder report that the disorder is more common among married.[5,18,19] Almost half of the patients with bipolar disorder in Türkiye have

an educational background of 5 years or less.20 Our data are consistent with previous studies.

Our study found that the mean age of the patients was 46.60 years. Although bipolar disorder is expected more frequently at a younger age, similar studies showed that the mean age of patients with bipolar disorder ranges from 40 to 43 years.[4,5,10-12,19] In a study conducted in Poland, the mean age was reported to be 46.2 years, which is quite similar to our data.[11]

Polypharmacy is more common at younger ages in bipolar disorder.[4] However, we found that the rate of polypharmacy was higher in patients aged 55 to 64 years. In our study, the duration of the disorder was high, and the number of patients with a duration of 10 years or more was high. So, this study involved a chronic group of patients. Bipolar disorder evolves more severely in chronic patients, who have more frequent manic episodes, the increased frequency of polypharmacy is not surprising.

The mean number of drugs used daily was 2.3±10. Of the 20-33% of bipolar patients are reported to take 4 or more psychotropic drugs during hospitalization.[14] In parallel with our study, the studies conducted with outpatients showed that the mean number of drugs used daily varies between 2.4 and 3.8.1,8,12 The clinical stability of patients included in this study may be the reason for decreased number of drugs used daily.

Bipolar disorder and polypharmacy

We found that the rate of polypharmacy was 79.40% among clinically stable bipolar outpatients. According to the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), a large-scale study on bipolar disorder, and the majority of whom are outpatients, 40% of the patients with bipolar disorder, use three or more drugs.[14] Various studies investigating rates of polypharmacy in bipolar disorder have found that the rate of polypharmacy ranges from 50% to 93.7%.[1,3-5,8,11-14] The rate of polypharmacy in our study is consistent with data in the literature.

A variety of drugs are used in the acute period and prophylactic treatment in bipolar disorder.[6] Both the broad range of symptoms and the recurrent, episodic, and heterogeneous nature of the disorder require combinations in treatment. As such, the likelihood of polypharmacy increases.[6,14-17] As well, studies suggest that no adequate response to monotherapy is achieved in the acute period, that monotherapy fails to reduce relapse rates and maintain remission, and that regimens with the combination of 2 or 3 drugs are more effective in achieving remission.[1,7,8] The present clinical practice shows that patients with bipolar disorder are treated on average with 3 to 4 different psychotropic drugs. Whilst its effectiveness remains largely unknown due to a lack of controlled studies, there is evidence from the United States and Europe that polypharmacy is frequently used.[3]

The most prevalent cause of polypharmacy in bipolar disorder is the failure in achieving remission.[16] The most comprehensive study conducted on bipolar disorder, the STEP-BD, revealed that, after a two-year follow-up period, 42% of symptomatic patients showed no improvement despite treatment.[14] It has recently been reported that polypharmacy is more potent in prophylactic treatment. The unavailability of an ideal MS agent for bipolar disorder has prompted clinicians to boost the treatment with a second ineffective or partially effective drug.[11] For these reasons, the use of combined drugs for bipolar disorder is now recommended.[15] Beyond these, polypharmacy is driven by many factors, such as the episodic nature of the bipolar disorder, high rates of recurrence in patients using only MS, comorbid psychiatric illnesses, attempts to control side effects, and a poor understanding of the pathophysiology of the disorder.[1,8]

The studies on current treatment guidelines for bipolar disorder have revealed that these guidelines are incoher-

ent and lacking in some respects. The guidelines state that patients with different clinical characteristics (e.g., with rapid cycles or a chronic course) are not considered, that psychiatric and medical comorbidities are ignored, and that no specific recommendations for particular purposes are made.[14] Polypharmacy is described as the treatment regimen that does not follow treatment guidelines but makes the greatest contribution to treatment for bipolar disorder.[21] The STEP-BD study found that the patients who received monotherapy were less than 20%.[22] Today, polypharmacy is recognized as the norm rather than an exception in the treatment of bipolar disorder.[10] Using two MSs or one MS with an atypical AP has now become a standard practice in the treatment of patients.[17]

Types of combinations

We found that the most preferred treatment for bipolar disorder was the combination of a MS and an AP drug. The combinations include at least one MS and one AP with a rate of 41.60%. There is evidence from randomized controlled studies that the combination of a MS and an atypical AP is more effective, especially in acute mania[11]. It appears that combinations vary according to clinicians' preferences or countries' economic policies on health care.[8,11,12] The studies from different countries reported that the most widely used type of polypharmacy was the combination of MS+AP, which is similar to our data.[1,10,11,13] Our results confirm previous evidence that the use of MS+AP in the treatment of bipolar disorder is more effective than the use of either drug alone.[1,23]

Types of drugs

We found that AP drugs were the most often preferred drugs in bipolar disorder, followed by MSs in the second, and ADs in the third (78.0%, 54.10%, and 43.50%, respectively). BDZs were found to be preferred minimally. The literature shows that MS use in bipolar disorder ranges from 82% to 92.4%, with AP ranging from 32.0% to 53.8%, AD from 15% to 66.7%, and BDZ from 7.8% to 42.5%.[1,5,8,11,12]

In our study, we found that the rates of MS and BDZ use are lower, whilst the rate of AD use is consistent with the literature, and the rate of AP use is higher than reported in the literature. There was a significant increase in the use of atypical APs and a decrease in the number of patients treated with MS between 1998 and 2009.[11] A recent study surveying treatment practice in bipolar disorder found that rates of MS use have decreased and the use of APs has increased in recent years.[6] Besides, a study conducted in our country in 2014 reported that APs were used for a longer period in patients with manic/hypomanic episodes and psychotic symptoms in bipolar disorder, and the use of APs became more common and the duration of use was prolonged.[19] Although our study did not consider the type of episode in the past and the presence of psychotic symptoms during the attack, the use of APs in preference to MSs may have been affected by the type of attack and the presence of psychotic symptoms.

Use of mood stabilizers

Our study showed that sodium valproate is more preferred than lithium. Although there are new treatment regimens available, lithium is still recognized as the most effective treatment for reducing the recurrence of episodes and is recommended as first-line therapy by the National Institute for Health and Care Excellence (NICE).[24] However, despite NICE recommendations, it is evident that lithium is not used sufficiently in clinical practice, where other mood stabilizers, and especially atypical APs, are becoming more popular.[2,6] Lithium can effectively prevent recurrences in only one-third of patients. Accordingly, many studies from a variety of countries confirmed that the drugs used in the treatment of bipolar disorder have undergone significant changes over time.[2] It is also reported that the preference for lithium has decreased over the years, antiepileptic and AP drugs have been prescribed more, and even atypical antipsychotics have replaced lithium.[2,25,29] On the other hand, sodium valproate is the most widely prescribed drug for bipolar disorder in certain countries.[10,11] Hence, the prevalence of sodium valproate use as MS among our

patients supports the view that preferences in bipolar disorder treatment have changed.

Use of antipsychotics

We found that the most frequently preferred drugs for the treatment of bipolar disorder were APs. The most important development in the past was the awareness that lithium, valproate, and carbamazepine have a mood-stabilizing effect on bipolar disorder. Yet, the proof that atypical APs are effective in the treatment of acute attacks, in the late 21st century, has led to these drugs being referred to as second-generation mood stabilizers.[11] As a consequence, the preference for atypical APs in the treatment of bipolar disorder has dramatically increased.[25] Atypical APs are now recommended for the acute and maintenance phases of the disorder.[5]

Quetiapine was found to be the most preferred AP drug in our patients, followed by olanzapine and aripiprazole, respectively. The Turkish Psychiatric Association's Guidelines for the Treatment of Bipolar Disorder indicate that quetiapine is superior to the combined or single use of lithium and sodium valproate in the prophylactic treatment. When used alone, its antidepressant effect is superior to that of lithium, along with similar efficacy to lithium in preventing mania or hypomania.[26] Unlike other atypical APs, quetiapine works well in all stages of bipolar disorder (manic/mixed episode/depression), in both acute and maintenance treatment. Therefore, treatment guidelines recommend the use of quetiapine as first- and second-line treatment for all stages of bipolar disorder.[11,25] The fact that quetiapine was the most frequently preferred AP drug in our study is consistent with treatment guidelines, which suggests that it may be the right choice for the treatment of bipolar disorder.

Use of antidepressants

In our study, the rate of AD use in bipolar disorder was 43.50%. If AD is required in bipolar disorder, it is recommended that the duration of use be kept short and tapered quickly once improvement is achieved.[27] However, it is also reported that 15-20% of patients become depressed again after discontinuing AD, indicating the need for AD.1 A large-scale national study from Denmark reported that the rate of AD use ranged from 40% to 61.5% across patient groups.[25] However, the STEP-BD study, revealed that the rate of AD use in bipolar disorder was 40.6%.[28] Although the rate of AD use we obtained appears high, it is consistent with the rates reported previously.

The most frequently prescribed AD group was SSRIs (21.50%), with the most frequently preferred AD was paroxetine. The rate of SSRI use was reported as about 29% by Holzapfel et al., and 21.6% in the STEP-BD study.[1,28] The guidelines for the treatment of bipolar disorder recommend the use of SSRIs owing to the higher risk of rapid cycling or manic switch with newer antidepressants and tricyclic agents.[25] Whereas we did not evaluate psychiatric comorbidity, the reason that paroxetine was preferred more may be attributed to the fact that our patients with bipolar disorder were accompanied by anxiety disorders.

We find that the rates of use of ADs in both the SSRI and non-SSRI groups are close to each other. The high rate of use of ADs other than SSRIs appears to be risky in terms of rapid cycling or manic switch. This may imply that physicians lack sufficient information about the risks of attack or are ignorant of the risk.

Use of benzodiazepines

The rate of BDZ use was quite low (3.80%). The rates of BDZ use in bipolar disorder have reported the rates between 5% and 40%.[5,11] The use of BDZ in bipolar disorder stems either from the prolongation of the polypharmacy process or from the inability to adequately control the attacks. BDZs are typically used in the acute attack period.[24] The predominance of lorazepam use as a BDZ drug in our study confirms this information. The low rates of BDZ use in this study may be linked to clinically stable patients included in the study.

This study has some limitations. First, conditions such as comorbid psychiatric disorders that may cause polypharmacy have not been evaluated. Second, the severity of the disorder, the number and types of attacks in the past, and the presence of psychotic symptoms accompanying the attack were not examined. A further limitation is the lack of assessment of drug compliance. Addressing these issues in future studies may help to establish a causal relationship in the preference for combinations and to develop more rational treatment protocols. Finally, this study does not include any hypotheses as it is a prevalence study examining the polypharmacy rates of a group of patients with bipolar disorder.

CONCLUSION

This study presents an example of bipolar disorder treatment practices, drug and combination preferences reflecting Turkiye. In this study, the rate of polypharmacy was found to be high. Therefore, psychiatrists in our country are advised to be careful about drug-drug interactions. In addition, it should be kept in mind that the use of multiple drugs may impair drug compliance in a disease such as bipolar disorder that requires regular drug treatment. Future studies are needed to cover the effect of polypharmacy on drug compliance and drug-drug interactions in polypharmacy in bipolar disorder.

Author Contributions

Study design: NA, Data collection: FÇ, Statistical evaluation: NA, Supervision: FÇ and NK, Writing – original draft: NA Writing – review & editing: NA, FÇ, NK.

Conflict of Interest

The authors have no conflicts of interest to declare.

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